from the group consisting of polystyrene, polyethylene, cellulose, polyacrylate, polyacrylamide, silica and glass.

## REMARKS

On January 23, 2002, a Continuation Prosecution Application (CPA) was filed in this case. Prior to the examination of the CPA, Applicants submit this Preliminary Amendment, canceling claims of 98 to 128 and adding new claims 129 to 159. Accordingly, claims 129 to 159 are now pending. The Amendment is being submitted to present the claims in a better form and to address the rejections and objections set forth in the July 23, 2001 Office Action in the parent case.

Before proceeding with the response, Applicants wish to thank the Examiner for the courtesies extended during the telephone interview of November 21, 2001, during which the rejections and objections pending in this case were discussed. Applicants' position as to those issues, communicated to the Examiner during that interview, are reiterated in this Amendment.

### Election/Restriction Requirement

In paragraphs 5 to 7 of the Office Action, the Examiner sets forth the restriction requirements. First, the Examiner requests that the earlier verbal election of Group I claims, along with the species election of nucleotides (for compound), binding to a probe (for property) and static planar array (for array) be confirmed. Second, the Examiner points out that claims 114-115 and 117-120 are withdrawn from consideration as being directed to non-elected species of the compound. Third, claim 126 is objected to as drawn to a product (a chemical library), which is allegedly distinct from the originally elected process claims.

In response, Applicants confirm election of Group I claims, and also the species election of

nucleotides (for compound), binding to a probe (for property) and static planar array (for array). As for the species elections, however, Applicants reserve the right to add claims to additional non-elected species once the generic claims directed to a compound library is allowed. MPEP 809.02. Accordingly, Applicants reserve the right to add additional species, including the compounds that are now recited in claims 151 to 153. As for claim 126, this claim has been canceled without prejudice.

Paragraphs 12 to 17 of the Office Action contain 35 U.S.C. §112 rejections, including the rejection of claim 106 for allegedly containing an incorrect chemical structure for a fluorescent compound. In addition, claims 98-128 are rejected because the phrase "bit of binary code" is allegedly vague.

Applicants respectfully maintain that the claims as amended overcome most of the rejections set forth in Paragraphs 12 to 17. As for the rejection of claim 106 based on the compound structure, and rejection of claims 98 to 128 for the use of the phrase "bit of binary code," Applicants respectfully traverse. In connection with the chemical structure, now present in claims 141, Applicants have verified the structure from the manufacturer's website and enclose that information for the Examiner's review. As for the phrase "bit of binary code," Applicants maintain that the phrase is not vague nor indefinite.

Claims 129 to 159 provide that a combinatorial library is synthesized on solid supports by a series of reaction steps in which the components of a compound are added to the solid supports. The identity of the added component is encoded by attaching a spectrally distinguishable fluorophore tag that is uniquely associated with each component and reaction step. The encoding strategy of claims 129 to 159 involves a fluorophore-tag-based binary code, wherein each fluorophore tag "represents one or more bits of a binary code." The term "bit" (the standard abbreviation for "binary digit") refers to a unit or element of a binary code. Each fluorophore tag comprises zero,

one, or more than one fluorescent dye(s) and represents one bit, or a set of bits, uniquely associated with a specific reaction step and component. For example, as a way of illustration without any intention of limiting the scope of the invention,

(i) a reaction step with two components, a and b, could be encoded by a fluorophore tag comprising zero or one fluorescent dye, d, representing one bit, as follows:

a = 1 unit of d;

b = 0 unit of d;

and

(ii) a reaction step with four components, a-d, could be encoded by a fluorophore tag comprising zero, one or two fluorescent dyes, $d_1$ and $d_2$, representing two bits, as follows:

a = 1 unit of $d_1$, 1 unit of $d_2$;

b = 1 unit of $d_1$, 0 unit of $d_2$;

c = 0 unit of $d_1$, 1 unit of $d_2$;

d = 0 units of $d_1$, 0 units of $d_2$;

and

(iii) a reaction step with eight components, a-h, could be encoded by a fluorophore tag comprising zero, one, two, three fluorescent dyes, $d_1$-$d_3$, representing three bits, as follows:

a = 1 unit of $d_1$, 1 unit of $d_2$, 1 unit of $d_3$;

b = 1 unit of $d_1$, 1 unit of $d_2$, 0 unit of $d_3$;

c = 1 unit of $d_1$, 0 unit of $d_2$, 1 unit of $d_3$;

d = 0 unit of $d_1$, 1 unit of $d_2$, 1 unit of $d_3$;

e = 1 unit of $d_1$, 0 unit of $d_2$, 0 unit of $d_3$;

f = 0 unit of $d_1$, 0 unit of $d_2$, 1 unit of $d_3$;

g = 0 unit of $d_1$, 1 unit of $d_2$, 0 unit of $d_3$;

h = 0 unit of $d_1$, 0 unit of $d_2$, 0 unit of $d_3$.

and so forth.

In addition, Applicants respectfully submit that the term "bit of binary code," is known in context of chemical libraries. Applicants direct the Examiner's attention to Ohlmeyer et al., PNAS, volume 90, pp. 10922 - 10926 (1993), which provides an example of the binary coding strategy where "bits" of binary code are added. See page 10923, right column, last paragraph, to page 10924, left column. Although Olhmeyer describes tags and a decoding strategy that are different from the claimed invention, it supports Applicants' position that the term "bit of binary code" is known and understood by those skilled in the art.

**Rejections Under 35 U.S.C. §102(b)**

Claims 98 to 128 are rejected under 35 U.S.C. §102(b) as being anticipated by WO93/06121 to Dower et al ("Dower"). Applicants respectfully traverse the rejections.

Claims 129 to 159 are directed to a method of identifying a compound of interest from a library of compounds which utilizes a novel combination of an encoding and a decoding scheme. Specifically, the claimed method comprises preparation of a library of compounds using a divide-couple-recombine strategy (DCR strategy) in which the identity of each of the component added in generating a compound is encoded by also attaching a spectrally distinguishable fluorophore tag uniquely associated with each component. Once the library is produced, it is screened for the presence of a compound having a selected property of interest, and the tag associated with the property of interest is decoded to determine which components were added during the compound synthesis and the reaction sequence of said components. The information thus obtained allows the identity of the compound to be determined.

The encoding-decoding combination of the claimed method provides significant advantages. For example, because the solid supports of interest need not be isolated from other solid supports, and

because the tags need not be cleaved from the solid support in the decoding process, the claimed method is more efficient in terms of time and labor required for decoding of the compound of interest in a chemical library. See pages 3-4 of the Specification.

Dower does not anticipate the claimed invention, at least because it does not disclose decoding of the tags without physically isolating the solid supports of interest from other solid supports. This difference was recognized by the Examiner on paragraphs 18 and 22 of the Office Action.

In paragraph 19 of the Office Action, the Examiner asserts that Dower "teaches the use of fluorophore dyes in binary code method." Applicants respectfully disagree. On pages 24 to 26 of Dower, it is stated that the nucleotide bases "could be used in a binary code" when oligonucleotide identifier tag is used. This binary coding strategy therefore pertains to nucleotide bases and not to fluorophore tags.

As for fluorophores, Dower provides as follows:

> In one embodiment, each bead or other solid support in the library incorporates a variety of fluorophores, or other light addressable type of molecules, the spectral properties of which can be changed and therefore used to store information. In one such mode, a bead incorporates a variety of fluorophores, each of which can be selectively photobleached and so rendered incapable of fluorescence or of diminished fluorescence [emphasis added].

See page 20, lines 25-30.

Accordingly, what Dower provides deals with changing the spectral properties of fluorophores ( e.g., by photobleaching), thus is different from the claimed invention.

In view of the foregoing, Applicants respectfully maintain that the claims are not anticipated by Dower, and request that the rejections be reconsidered and withdrawn.

**Rejections Under 35 U.S.C. §103**

Claims 98 to 128 are rejected under 35 U.S.C. §103 as being unpatentable over U.S. Patent No. 5,968,736 to Still et al. ("Still"). Applicants respectfully traverse these rejections.

Still does not render obvious the claimed invention, at least because it does not teach or suggest that the decoding be carried out without removing the solid supports of interest from the mixture and without cleaving the identifier tag from the solid supports for further analysis. Rather, as with Dower, Still teaches that the identification be carried out by isolating the solid supports of interest from other solid supports, and by cleaving the tags from the solid supports for further off-line analysis. See column 6, lines 26 to 41; and column 17, lines 2 to 18. Still provides that the tag is attached to a cleavable linker, which is in turn attached to the solid support, such that the tag may be released from the solid support by cleaving the linker. See column 4, lines 8-25. It further addresses the role that the detachment of the tag plays in the method described therein:

> Importantly, the present method employs tags which are detachable from a ligand or compound synthesized also for the purpose of decoding. Such detachability allows the tags to be distinguished on more than one basis; in particular, they can be separated (e.g., on the basis of chromatographic retention time) and then analyzed (e.g., a second basis is a spectral property such as mass spectroscopy m/e, or electrophoricity). Having multiple bases for distinction allows the encoding of large amounts of information with a small number of tags.

See column 6, lines 26 to 35.

Accordingly, Still does not teach or suggest that a decoding of the identify of the compound of interest in a chemical library may be carried out without detaching the tags from the solid supports and without removing the solid supports of interest from other solid supports. The claimed invention, which teaches such a method, provides advantages that are not present in Still. By allowing decoding of the tags without physical separation, the present invention provides a

method that does not involve the time and labor associated with the offline-line chemical analysis of the tags.

In view of the foregoing reasons, Applicants respectfully maintain that the claims are patentable over Still.

Claims 98 to 128 are rejected under 35 U.S.C. §103 as being unpatentable over Dower in view of Metzeker et al. Applicants respectfully traverse these rejections.

The claims are not rendered obvious by Dower, at least for the reasons previously set forth in this response. Dower does not teach or suggest the decoding of the tags of a compound of interest in the chemical library without removing the solid supports of interest from the mixture, and Metzeker does not remedy this deficiency. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of these rejections.

In view of the foregoing amendments and remarks, Applicants maintain that the application is in condition for allowance. An early and favorable action on the merits is earnestly solicited.

If the Examiner is of the view that there are any issues which remain pending after this Amendment, an interview is respectfully requested prior to issuance of any paper other than a

Notice of Allowance; and the Examiner is respectfully requested to contact the undersigned by telephone to arrange a mutually convenient time for the interview.

Respectfully submitted,

Julie Bowker

Julie Bowker
Registration No. 37,870
Attorney for Applicants

Julie Bowker
60 East 42nd Street, Suite 2918
New York, NY 10165
Tel : (212) 867-3171
Fax : (212) 867-3174

# Structure for A-10236

## Alexa Fluor® 532 Protein Labeling Kit

### COMPONENT A: Alexa Fluor® 532 carboxylic acid, succinimidyl ester

**Molecular Formula:** $C_{34}H_{33}N_3O_{11}S_2$

**Molecular Weight:** 723.77

**CAS Number/Name:** N/A